BWP - Biological Weapons

Information obtained from USAMRIID's Medical Management of Biological Casualties Handbook, Fourth Edition, February 2001

The information contained in these codes can be used to guide patient education and should not be relied upon as a source for guiding therapeutic decisions. For all questions related to treatment and vaccinations, please contact the most recent update of the USAMRIID's Medical Management of Biological Casualties Handbook, your state guidelines, and/or your hospital's policy and procedures.

BWP-C COMPLICATIONS

OUTCOME: The patient/family will understand the potential consequences of exposure to a biological weapon and will understand the effects, consequences possible as a result of this exposure, failure to manage the exposure, or as a result of treatment.

STANDARDS:

1. Discuss common or significant complications that may occur after exposure to biological weapons as appropriate.
2. Discuss common or significant complications which may be prevented by fully participating in the treatment regimen.
3. Discuss common or significant complications which may result from treatment(s).

BWP-CUL CULTURAL/SPIRITUAL ASPECTS OF HEALTH

OUTCOME: The patient/family will understand the impact and influences cultural and spiritual traditions, practices, and beliefs have on health and wellness.

STANDARDS:

1. Explain that the outcome of disease processes may be influenced by choices related to health and lifestyles, e.g., diet, exercise, sleep, stress management, hygiene, full participation in the medical plan. (Stoic Fatalism)
2. Discuss the potential role of cultural/spiritual traditions, practices, and beliefs in achieving and maintaining health and wellness.
3. Explain that traditional medicines/treatments should be reviewed with the healthcare provider to determine if there are interactions with prescribed treatment.
4. Explain that the medical treatment plan must be followed as prescribed to be effective and that some medications/treatments take time to demonstrate effectiveness.

5. Discuss that traditions, such as sweat lodges, may affect some conditions in detrimental ways. Healing customs or using a traditional healer may have a positive effect on the patient's condition.
6. Refer to clergy services, traditional healers, or other culturally appropriate resources.

BWP-DP DISEASE PROCESS

OUTCOME: The patient/family will understand the expected course of disease resulting from exposure to the biological weapon.

STANDARDS:

1. Discuss the current information about the suspected biological weapon including the time-course, clinical features, and pathophysiology.
2. Discuss the signs/symptoms and usual progression of the suspected biological weapon.
    a. **Anthrax:** The incubation period is generally 1–6 days, although longer periods have been noted. Fever, malaise, fatigue, cough and mild chest discomfort progresses to severe respiratory distress with dyspnea, diaphoresis, stridor, cyanosis, and shock. Death typically occurs within 24–36 hours after onset of severe symptoms. Anthrax presents three somewhat distinct clinical syndromes in humans: cutaneous, inhalational, and gastrointestinal disease. The cutaneous form (also referred to as a malignant pustule) occurs most frequently on the hands and forearms of persons working with infected livestock. It begins as a papule followed by formation of a fluid-filled vesicle. The vesicle typically dries and forms a coal-black scab (eschar), hence the term anthrax (from the Greek for coal). This local infection can occasionally disseminate into a fatal systemic infection. Gastrointestinal anthrax is rare in humans and is contracted by the ingestion of insufficiently cooked meat from infected animals. Endemic inhalational anthrax, known as Woolsorters' disease, is also a rare infection contracted by inhalation of the spores. It occurs mainly among workers in an industrial
    b. **Brucellosis:** Brucellosis has a low mortality rate (5% of untreated cases), with rare deaths caused by endocarditis or meningitis. Also, given that the disease has a relatively long and variable incubation period (5–60 days), and that many naturally occurring infections are asymptomatic, its usefulness as a weapon may be diminished. Large aerosol doses, however, may shorten the incubation period and increase the clinical attack rate, and the disease is relatively prolonged, incapacitating, and disabling in its natural form. Brucellosis, also known as "undulant fever," typically presents as a nonspecific febrile illness resembling influenza. Fever, headache, myalgias, arthralgias, back pain, sweats, chills, generalized weakness, and malaise are common complaints. Cough and pleuritic chest

pain occurs in up to 20 percent of cases, but acute pneumonitis is unusual, and pulmonary symptoms may not correlate with radiographic findings. The chest x-ray is often normal, but may show lung abscesses, single or miliary nodules, bronchopneumonia, enlarged hilar lymph nodes, and pleural effusions. Gastrointestinal symptoms (anorexia, nausea, vomiting, diarrhea and constipation) occur in up to 70 percent of adult cases, but less frequently in children. Ileitis, colitis, and granulomatous or mononuclear infiltrative hepatitis may occur, with hepato- and splenomegaly present in 45–63 percent of cases. Lumbar pain and tenderness can occur in up to 60% of brucellosis cases and are sometimes due to various osteoarticular infections of the axial skeleton. Vertebral osteomyelitis, intervertebral disc space infection, paravertebral abscess, and sacroiliac infection occur in a minority of cases, but may be a cause of chronic symptoms. Consequently, persistent fever following therapy or the prolonged presence of significant musculoskeletal complaints should prompt CT or MR imaging. 99m Technetium and 67 Gallium scans are also reasonably sensitive means for detecting sacroiliitis and other axial skeletal infections. Joint involvement in brucellosis may vary from pain to joint immobility and effusion. While the sacroiliac joints are most commonly involved, peripheral joints (notably, hips, knees, and ankles) may also be affected. Meningitis complicates a small minority of brucellosis cases, and encephalitis, peripheral neuropathy, radiculoneuropathy and meningovascular syndromes have also been observed in rare instances. Behavioral disturbances and psychoses appear to occur out of proportion to the height of fever, or to the amount of overt CNS disease. This raises questions about an ill-defined neurotoxic component of brucellosis.

c. **Glanders and Melioidosis:** Incubation period ranges from 10–14 days after inhalation. Onset of symptoms may be abrupt or gradual. Inhalational exposure produces fever (common in excess of 102°F), rigors, sweats, myalgias, headache, pleuritic chest pain, cervical adenopathy, hepatosplenomegaly, and generalized papular / pustular eruptions. Acute pulmonary disease can progress and result in bacteremia and acute septicemic disease. Both diseases are almost always fatal without treatment. Both glanders and melioidosis may occur in an acute localized form, as an acute pulmonary infection, or as an acute fulminant, rapidly fatal, sepsis. Combinations of these syndromes may occur in human cases. Also, melioidosis may remain asymptomatic after initial acquisition, and remain quiescent for decades. However, these patients may present with active melioidosis years later, often associated with an immune-compromising state. Aerosol infection produced by a BW weapon containing either B. mallei or B. pseudomallei could produce any of these syndromes. The incubation period ranges from 10–14 days, depending on the inhaled dose and agent virulence. The septicemic form begins suddenly with fever, rigors, sweats, myalgias, pleuritic chest pain, granulomatous or necrotizing lesions, generalized erythroderma, jaundice, photophobia, lacrimation, and diarrhea. Physical examination may reveal

fever, tachycardia, cervical adenopathy and mild hepatomegaly or splenomegaly. Blood cultures are usually negative until the patient is moribund. Mild leukocytosis with a shift to the left or leukopenia may occur. The pulmonary form may follow inhalation or arise by hematogenous spread. Systemic symptoms as described for the septicemic form occur. Chest radiographs may show miliary nodules (0.5–1.0 cm) and/or a bilateral bronchopneumonia, segmental, or lobar pneumonia, consolidation, and cavitating lung lesions. Acute infection of the oral, nasal, and/ or conjunctival mucosa can cause mucopurulent, blood-streaked discharge from the nose, associated with septal and turbinate nodules and ulcerations. If systemic invasion occurs from mucosal or cutaneous lesions then a papular and / or pustular rash may occur that can be mistaken for smallpox (another possible BW agent). Evidence of dissemination of these infections includes the presence of skin pustules, abscesses of internal organs, such as liver and spleen, and multiple pulmonary lesions. This form carries a high mortality, and most patients develop rapidly progressive septic shock. The chronic form is unlikely to be present within 14 days after a BW aerosol attack. It is characterized by cutaneous and intramuscular abscesses on the legs and arms. These lesions are associated with enlargement and induration of the regional lymph channels and nodes. The chronic form may be asymptomatic, especially with melioidosis. There have been cases associated with the development of steomyelitis, brain abscess, and meningitis.

d. **Plague:** Pneumonic plague begins after an incubation period of 1–6 days, with high fever, chills, headache, malaise, followed by cough (often with hemoptysis), progressing rapidly to dyspnea, stridor, cyanosis, and death. Gastrointestinal symptoms are often present. Death results from respiratory failure, circulatory collapse, and a bleeding diathesis. Bubonic plague, featuring high fever, malaise, and painful lymph nodes (buboes) may progress spontaneously to the septicemic form (septic shock, thrombosis, DIC) or to the pneumonic form. Plague normally appears in three forms in man: bubonic, septicemic, and pneumonic. The bubonic form begins after an incubation period of 2–10 days, with acute and fulminant onset of nonspecific symptoms, including high fever, malaise, headache, myalgias, and sometimes nausea and vomiting. Up to half of patients will have abdominal pain. Simultaneous with or shortly after the onset of these nonspecific symptoms, the bubo develops – a swollen, very painful, infected lymph node. Buboes are normally seen in the femoral or inguinal lymph nodes as the legs are the most commonly flea-bitten part of the adult human body. The liver and spleen are often tender and palpable. One quarter of patients will have various types of skin lesions: a pustule, vesicle, eschar or papule (containing leukocytes and bacteria) in the lymphatic drainage of the bubo, and presumably representing the site of the inoculating flea bite. Secondary septicemia is common, as greater than 80 percent of blood cultures are positive for the organism in patients with bubonic plague. However, only about a quarter of bubonic plague patients

progress to clinical septicemia. In those that do progress to secondary septicemia, as well as those presenting septicemic but without lymphadenopathy (primary septicemia), the symptoms are similar to other Gram-negative septicemias: high fever, chills, malaise, hypotension, nausea, vomiting, and diarrhea. However, plague septicemia can also produce thromboses in the acral vessels, with necrosis and gangrene, and DIC. Black necrotic appendages and more proximal purpuric lesions caused by endotoxemia are often present. Organisms can spread to the central nervous system, lungs, and elsewhere. Plague meningitis occurs in about 6% of septicemic and pneumonic cases. Pneumonic plague is an infection of the lungs due to either inhalation of the organisms (primary pneumonic plague), or spread to the lungs from septicemia (secondary pneumonic plague). After an incubation period varying from 1 to 6 days for primary pneumonic plague (usually 2–4 days, and presumably dose-dependent), onset is acute and often fulminant. The first signs of illness include high fever, chills, headache, malaise, and myalgias, followed within 24 hours by a cough with bloody sputum. Although bloody sputum is characteristic, it can sometimes be watery or, less commonly, purulent. Gastrointestinal symptoms, including nausea, vomiting, diarrhea, and abdominal pain, may be present. Rarely, a cervical bubo might result from an inhalational exposure. The chest X-ray findings are variable, but most commonly reveal bilateral infiltrates, which may be patchy or consolidated. The pneumonia progresses rapidly, resulting in dyspnea, stridor, and cyanosis. The disease terminates with respiratory failure, and circulatory collapse. Nonspecific laboratory findings include a leukocytosis, with a total WBC count up to 20,000 cells with increased bands, and greater than 80 percent polymorphonuclear cells. One also often finds increased fibrin split products in the blood indicative of a low-grade DIC. The BUN, creatinine, ALT, AST, and bilirubin may also be elevated, consistent with multi-organ failure. In man, the mortality of untreated bubonic plague is approximately 60 percent (reduced to <5% with prompt effective therapy), whereas in untreated pneumonic plague the mortality rate is nearly 100 percent, and survival is unlikely if treatment is delayed beyond 18 hours of infection. In the U.S. in the past 50 years, 4 of the 7 pneumonic plague patients (57%) died. Recent data from the ongoing Madagascar epidemic, which began in 1989, corroborate that figure; the mortality associated with respiratory involvement was 57%, while that for bubonic plague was 15%.

e. **Q-Fever:** Fever, cough, and pleuritic chest pain may occur as early as ten days after exposure. Patients are not generally critically ill, and the illness lasts from 2 days to 2 weeks. Following the usual incubation period of 2–14 days, Q fever generally occurs as a self-limiting febrile illness lasting 2 days to 2 weeks. The incubation period varies according to the numbers of organisms inhaled, with longer periods between exposure and illness with lower numbers of inhaled organisms (up to forty days in some cases). The disease generally presents as an acute non-differentiated febrile illness,

with headaches, fatigue, and myalgias as prominent symptoms. Physical examination of the chest is usually normal. Pneumonia, manifested by an abnormal chest x-ray, occurs in half of all patients, but only around half of these, or 28 percent of patients, will have a cough (usually non-productive) or rales. Pleuritic chest pain occurs in about one-fourth of patients with Q fever pneumonia. Chest radiograph abnormalities, when present, are patchy infiltrates that may resemble viral or mycoplasma pneumonia. Rounded opacities and adenopathy have also been described. Approximately 33 percent of Q fever cases will develop acute hepatitis. This can present with fever and abnormal liver function tests with the absence of pulmonary signs and symptoms. Uncommon complications include chronic hepatitis, culture-negative endocarditis, aseptic meningitis, encephalitis and osteomyelitis. Most patients who develop endocarditis have pre-existing valvular heart disease.

f. **Tularemia:** Ulceroglandular tularemia presents with a local ulcer and regional lymphadenopathy, fever, chills, headache and malaise. Typhoidal tularemia presents with fever, headache, malaise, substernal discomfort, prostration, weight loss and a non-productive cough. After an incubation period varying from 1–21 days (average 3–5 days), presumably dependent upon the dose of organisms, onset is usually acute. Tularemia typically appears in one of six forms in man depending upon the route of inoculation: typhoidal, ulceroglandular, glandular, oculoglandular, oropharyngeal, and pneumonic tularemia. In humans, as few as 10 to 50 organisms will cause disease if inhaled or injected intradermally, whereas approximately 10 organisms are required with oral challenge. Typhoidal tularemia (5–15 percent of naturally acquired cases) occurs mainly after inhalation of infectious aerosols, but can occur after intradermal or gastrointestinal challenge. F. tularensis would presumably be most likely delivered by aerosol in a BW attack and would primarily cause typhoidal tularemia. It manifests as fever, prostration, and weight loss, but unlike most other forms of the disease, presents without lymphadenopathy. Pneumonia may be severe and fulminant and can be associated with any form of tularemia (30% of ulceroglandular cases), but it is most common in typhoidal tularemia (80% of cases). Respiratory symptoms, substernal discomfort, and a cough (productive and non-productive) may also be present. Case fatality rates following a BW attack may be greater than the 1–3 % seen with appropriately treated natural disease. Case fatality rates are about 35% in untreated naturally acquired typhoidal cases. Ulceroglandular tularemia (75–85 percent of cases) is most often acquired through inoculation of the skin or mucous membranes with blood or tissue fluids of infected animals. It is characterized by fever, chills, headache, malaise, an ulcerated skin lesion, and painful regional lymphadenopathy. The skin lesion is usually located on the fingers or hand where contact occurs. Glandular tularemia (5–10 percent of cases) results in fever and tender lymphadenopathy but no skin ulcer. Oculoglandular tularemia (1–2 percent of cases) occurs after inoculation of the conjunctivae by

contaminated hands, splattering of infected tissue fluids, or by aerosols. Patients have unilateral, painful, purulent conjunctivitis with preauricular or cervical lymphadenopathy. Chemosis, periorbital edema, and small nodular lesions or ulcerations of the palpebral conjunctiva are noted in some patients. Oropharyngeal tularemia refers to primary ulceroglandular disease confined to the throat. It produces an acute exudative or membranous pharyngotonsillitis with cervical lymphadenopathy. Pneumonic tularemia is a severe atypical pneumonia that may be fulminant and with a high case fatality rate if untreated. It can be primary following inhalation of organisms or secondary following hematogenous / septicemic spread. It is seen in 30-80 percent of the typhoidal cases and in 10–15 percent of the ulceroglandular cases. The case fatality rate without treatment is approximately 5 percent for the ulceroglandular form and 35 percent for the typhoidal form. All ages are susceptible, and recovery is generally followed by permanent immunity.

g. **Smallpox:** Clinical manifestations begin acutely with malaise, fever, rigors, vomiting, headache, and backache. 2–3 days later lesions appear which quickly progress from macules to papules, and eventually to pustular vesicles. They are more abundant on the extremities and face, and develop synchronously. The incubation period of smallpox averaged 12 days, although it could range from 7–19 days following exposure. Clinical manifestations begin acutely with malaise, fever, rigors, vomiting, headache, and backache; 15% of patients developed delirium. Approximately 10% of light-skinned patients exhibited an erythematous rash during this phase. Two to three days later, an enanthem appears concomitantly with a discrete rash about the face, hands, and forearms. Following eruptions on the lower extremities, the rash spread centrally to the trunk over the next week. Lesions quickly progressed from macules to papules, and eventually to pustular vesicles. Lesions were more abundant on the extremities and face, and this centrifugal distribution is an important diagnostic feature. In distinct contrast to varicella, lesions on various segments of the body remain generally synchronous in their stages of development. From 8 to 14 days after onset, the pustules form scabs that leave depressed depigmented scars upon healing. Although variola concentrations in the throat, conjunctiva, and urine diminish with time, virus can be readily recovered from scabs throughout convalescence. Therefore, patients should be isolated and considered infectious until all scabs separate. For the past century, two distinct types of smallpox were recognized. Variola minor was distinguished by milder systemic toxicity and more diminutive pox lesions, and caused 1% mortality in unvaccinated victims. However, the prototypical disease variola major caused mortality of 3% and 30% in the vaccinated and unvaccinated, respectively. Other clinical forms associated with variola major, flat-type and hemorrhagic type smallpox were notable for severe mortality. A naturally occurring relative of variola, monkey pox, occurs in Africa, and is clinically indistinguishable from smallpox with the exception of a lower

case fatality rate and notable enlargement of cervical and inguinal lymph nodes.

h. **Venezuelan Equine Encephalitis:** Incubation period 1–6 days. Acute systemic febrile illness with encephalitis developing in a small percentage (4% children; < 1% adults). Generalized malaise, spiking fevers, rigors, severe headache, photophobia, and myalgias for 24–72 hours. Nausea, vomiting, cough, sore throat, and diarrhea may follow. Full recovery from malaise and fatigue takes 1–2 weeks. The incidence of CNS disease and associated morbidity and mortality would be much higher after a BW attack. Susceptibility is high (90-100%), and nearly 100% of those infected develop overt illnesses. The overall case fatality rate for VEE is <1%, although it is somewhat higher in the very young or aged. Recovery from an infection results in excellent short-term and long-term immunity. VEE is primarily an acute, incapacitating, febrile illness with encephalitis developing in only a small percentage of the infected population. Most VEE infections are mild (EEE and WEE are predominantly encephalitis infections). After an incubation period from 1–6 days, onset is usually sudden. The acute phase lasts 24–72 hours and is manifested by generalized malaise, chills, spiking high fevers (38˚C-40.5˚C), rigors, severe headache, photophobia, and myalgias in the legs and lumbosacral area. Nausea, vomiting, cough, sore throat, and diarrhea may follow. Physical signs include conjunctival injection, erythematous pharynx and muscle tenderness. Patients would be incapacitated by malaise and fatigue for 1–2 weeks before full recovery. During natural epidemics, approximately 4% of infected children (<15 years old) and less than 1% of adults will develop signs of severe CNS infection (35% fatality for children and 10% for adults). Adults rarely develop neurologic complications during natural infections. Experimental aerosol challenges in animals suggest that the incidence of CNS disease and associated morbidity and mortality would be much higher after a BW attack, as the VEE virus would infect the olfactory nerve and spread directly to the CNS. Mild CNS findings would include lethargy, somnolence, or mild confusion, with or without nuchal rigidity. Seizures, ataxia, paralysis, or coma follow more severe CNS involvement. VEE infection during pregnancy may cause encephalitis in the fetus, placental damage, abortion, or severe congenital neuroanatomical anomalies.

i. **Viral Hemorrhagic Fevers (VHF):** VHFs are febrile illnesses which can feature flushing of the face and chest, petechiae, bleeding, edema, hypotension, and shock. Malaise, myalgias, headache, vomiting, and diarrhea may occur in any of the hemorrhagic fevers. The clinical syndrome that these viruses may cause is generally referred to as viral hemorrhagic fever, or VHF. The target organ in the VHF syndrome is the vascular bed; accordingly, the dominant clinical features are usually due to microvascular damage and changes in vascular permeability. Not all infected patients develop VHF. There is both divergence and uncertainty about which host factors and viral strain characteristics might be

responsible for the mechanisms of disease. For example, an immunopathogenic mechanism has been identified for dengue hemorrhagic fever, which usually occurs among patients previously infected with a heterologous dengue serotype. Antibody directed against the previous strain enhances uptake of dengue virus by circulating monocytes. These cells express viral antigens on their surfaces. Lysis of the infected monocytes by cytotoxic T-cell responses results in the release of pro-inflammatory cytokines, pro-coagulants, and anticoagulants, which in turn results in vascular injury and permeability, complement activation, and a systemic coagulopathy. DIC has been implicated in Rift Valley, Marburg and Ebola fevers, but in most VHFs the etiology of the coagulopathy is multifactorial (e.g., hepatic damage, consumptive coagulopathy, and primary marrow injury to megakaryocytes). Common symptoms are fever, myalgia, and prostration. Physical examination may reveal only conjunctival injection, mild hypotension, flushing, and petechial hemorrhages. Full-blown VHF typically evolves to shock and generalized mucous membrane hemorrhage, and often is accompanied by evidence of pulmonary hematopoietic, and neurologic involvement. Renal insufficiency is proportional to cardiovascular compromise, except in HFRS, which features renal failure as an integral part of the disease process. Apart from epidemiologic and intelligence information, some distinctive clinical features may suggest a specific etiologic agent. While hepatic involvement is common among the VHFs, a clinical picture dominated by jaundice and other features of hepatitis is only seen in some cases of Rift Valley fever, Congo-Crimean, Marburg, and Ebola HFs, and yellow fever. Kyanasur Forest disease and Omsk hemorrhagic fever are notable for pulmonary involvement, and a biphasic illness with subsequent CNS manifestations. Among the arenavirus infections, Lassa fever can cause severe peripheral edema due to capillary leak, but hemorrhage is uncommon, while hemorrhage is commonly caused by the South American arenaviruses. Severe hemorrhage and nosocomial transmission are typical for Congo-Crimean HF. Retinitis is commonly seen in Rift Valley fever, and hearing loss is common among Lassa fever survivors. Because of their worldwide occurrence, additional consideration should be given to Hantavirus infections. Classic HFRS has a severe course that progresses sequentially from fever through hemorrhage, shock, renal failure, and polyuria. Nephropathia endemica features prominent fever, myalgia, abdominal pain, and oliguria, without shock or severe hemorrhagic manifestations. North American cases of Hantavirus Pulmonary Syndrome (HPS) due to the Sin Nombre virus lack hemorrhagic manifestations and renal failure, but nevertheless carry a very high mortality due to rapidly progressive and severe pulmonary capillary leak, which presents as ARDS. These syndromes may overlap. Subclinical or clinical pulmonary edema may occur in HFRS and nephropathia endemica, while HFRS has complicated HPS due to South American Hantaviruses and the Bayou and Black Creek Canal viruses in North

America. Mortality may be substantial, ranging from 0.2% percent for nephropathia endemica, to 50 to 90 percent among Ebola victims.

j. **Botulinum:** Usually begins with cranial nerve palsies, including ptosis, blurred vision, diplopia, dry mouth and throat, dysphagia, and dysphonia. This is followed by symmetrical descending flaccid paralysis, with generalized weakness and progression to respiratory failure. Symptoms begin as early as 12–36 hours after inhalation, but may take several days after exposure to low doses of toxin. The onset of symptoms of inhalation botulism usually occurs from 12 to 36 hours following exposure, but can vary according to the amount of toxin absorbed, and could be reduced following a BW attack. Recent primate studies indicate that the signs and symptoms may not appear for several days when a low dose of the toxin is inhaled versus a shorter time period following ingestion of toxin or inhalation of higher doses. Cranial nerve palsies are prominent early, with eye symptoms such as blurred vision due to mydriasis, diplopia, ptosis, and photophobia, in addition to other cranial nerve signs such as dysarthria, dysphonia, and dysphagia. Flaccid skeletal muscle paralysis follows, in a symmetrical, descending, and progressive manner. Collapse of the upper airway may occur due to weakness of the oropharyngeal musculature. As the descending motor weakness involves the diaphragm and accessory muscles of respiration, respiratory failure may occur abruptly. Progression from onset of symptoms to respiratory failure has occurred in as little as 24 hours in cases of severe food borne botulism. The autonomic effects of botulism are manifested by typical anticholinergic signs and symptoms: dry mouth, ileus, constipation, and urinary retention. Nausea and vomiting may occur as nonspecific sequelae of an ileus. Dilated pupils (mydriasis) are seen in approximately 50 percent of cases. Sensory symptoms usually do not occur. Botulinum toxins do not cross the blood/brain barrier and do not cause CNS disease. However, the psychological sequelae of botulism may be severe and require specific intervention. Physical examination usually reveals an afebrile, alert, and oriented patient. Postural hypotension may be present. Mucous membranes may be dry and crusted and the patient may complain of dry mouth or sore throat. There may be difficulty with speaking and swallowing. Gag reflex may be absent. Pupils may be dilated and even fixed. Ptosis and extraocular muscle palsies may also be present. Variable degrees of skeletal muscle weakness may be observed depending on the degree of progression in an individual patient. Deep tendon reflexes may be present or absent. With severe respiratory muscle paralysis, the patient may become cyanotic or exhibit narcosis from CO_2 retention.

k. **Ricin:** Acute onset of fever, chest tightness, cough, dyspnea, nausea, and arthralgias occurs 4 to 8 hours after inhalational exposure. Airway necrosis and pulmonary capillary leak resulting in pulmonary edema would likely occur within 18–24 hours, followed by severe respiratory distress and death from hypoxemia in 36–72 hours. The clinical picture in intoxicated victims would depend on the route of exposure. After aerosol

exposure, signs and symptoms would depend on the dose inhaled. Accidental sublethal aerosol exposures which occurred in humans in the 1940's were characterized by acute onset of the following symptoms in 4 to 8 hours: fever, chest tightness, cough, dyspnea, nausea, and arthralgias. The onset of profuse sweating some hours later was commonly the sign of termination of most of the symptoms. Although lethal human aerosol exposures have not been described, the severe pathophysiologic changes seen in the animal respiratory tract, including necrosis and severe alveolar flooding, are probably sufficient to cause death from ARDS and respiratory failure. Time to death in experimental animals is dose dependent, occurring 36–72 hours post inhalation exposure. Humans would be expected to develop severe lung inflammation with progressive cough, dyspnea, cyanosis and pulmonary edema. By other routes of exposure, ricin is not a direct lung irritant; however, intravascular injection can cause minimal pulmonary perivascular edema due to vascular endothelial injury. Ingestion causes necrosis of the gastrointestinal epithelium, local hemorrhage, and hepatic, splenic, and renal necrosis. Intramuscular injection causes severe local necrosis of muscle and regional lymph nodes with moderate visceral organ involvement.

l. **Staphylococcal Enterotoxin B:** Latent period of 3–12 hours after aerosol exposure is followed by sudden onset of fever, chills, headache, myalgia, and nonproductive cough. Some patients may develop shortness of breath and retrosternal chest pain. Patients tend to plateau rapidly to a fairly stable clinical state. Fever may last 2 to 5 days, and cough may persist for up to 4 weeks. Patients may also present with nausea, vomiting, and diarrhea if they swallow the toxin. Presumably, higher exposure can lead to septic shock and death. Symptoms of SEB intoxication begin after a latent period of 3–12 hours after inhalation, or 4–10 hours after ingestion. Symptoms include nonspecific flu-like symptoms (fever, chills, headache, myalgias), and specific features dependent on the route of exposure. Oral exposure results in predominantly gastrointestinal symptoms: nausea, vomiting, and diarrhea. Inhalation exposures produce predominantly respiratory symptoms: nonproductive cough, retrosternal chest pain, and dyspnea. GI symptoms may accompany respiratory exposure due to inadvertent swallowing of the toxin after normal mucocilliary clearance. Respiratory pathology is due to the activation of pro-inflammatory cytokine cascades in the lungs, leading to pulmonary capillary leak and pulmonary edema. Severe cases may result in acute pulmonary edema and respiratory failure. The fever may last up to five days and range from 103 to 106°F, with variable degrees of chills and prostration. The cough may persist up to four weeks, and patients may not be able to return to duty for two weeks. Physical examination in patients with SEB intoxication is often unremarkable. Conjunctival injection may be present, and postural hypotension may develop due to fluid losses. Chest examination is unremarkable except in the unusual case where pulmonary edema develops. The chest X-ray is also generally normal, but in severe cases

increased interstitial markings, atelectasis, and possibly overt pulmonary edema or an ARDS picture may develop.

m. **T-2 Mycotoxin**: Exposure causes skin pain, pruritus, redness, vesicles, necrosis and sloughing of the epidermis. Effects on the airway include nose and throat pain, nasal discharge, itching and sneezing, cough, dyspnea, wheezing, chest pain and hemoptysis. Toxin also produces effects after ingestion or eye contact. Severe intoxication results in prostration, weakness, ataxia, collapse, shock, and death. In a BW attack with trichothecenes, the toxin(s) can adhere to and penetrate the skin, be inhaled, and can be ingested. In the alleged yellow rain incidents, symptoms of exposure from all three routes coexisted. Contaminated clothing can serve as a reservoir for further toxin exposure. Early symptoms beginning within minutes of exposure include burning skin pain, redness, tenderness, blistering, and progression to skin necrosis with leathery blackening and sloughing of large areas of skin. Upper respiratory exposure may result in nasal itching, pain, sneezing, epistaxis, and rhinorrhea. Pulmonary/tracheobronchial toxicity produces dyspnea, wheezing, and cough. Mouth and throat exposure causes pain and blood tinged saliva and sputum. Anorexia, nausea, vomiting and watery or bloody diarrhea with crampy abdominal pain occurs with gastrointestinal toxicity. Eye pain, tearing, redness, foreign body sensation and blurred vision may follow ocular exposure. Skin symptoms occur in minutes to hours and eye symptoms in minutes. Systemic toxicity can occur via any route of exposure, and results in weakness, prostration, dizziness, ataxia, and loss of coordination. Tachycardia, hypothermia, and hypotension follow in fatal cases. Death may occur in minutes, hours or days. The most common symptoms are vomiting, diarrhea, skin involvement with burning pain, redness and pruritus, rash or blisters, bleeding, and dyspnea. A late effect of systemic absorption is pancytopenia, predisposing to bleeding and sepsis.

BWP-FU FOLLOW-UP

OUTCOME: The patient/family will understand the importance of follow-up and make a plan to keep follow-up appointments

STANDARDS:

1. Discuss the importance of follow-up care.
2. Discuss procedure for obtaining follow-up appointments.
3. Emphasize importance of keeping appointments and following the recommendations established by the city, county, state, and federal healthcare organizations.
4. Encourage the patient to seek further management if:
   a. Significant worsening of symptoms occurs

b. Symptoms last longer than expected

BWP-I INFORMATION

OUTCOME: The patient/family will receive information about biological weapons as appropriate

STANDARDS:

1. Identify the suspected biological weapon that the patient/family has been exposed to or that the patient/family is interested in learning about.

   a. **Anthrax:** Bacillus anthracis, the causative agent of Anthrax, is a gram-positive, sporulating rod. The spores are the usual infective form. Anthrax is primarily a zoonotic disease of herbivores, with cattle, sheep, goats, and horses being the usual domesticated animal hosts, but other animals may be infected. Humans generally contract the disease when handling contaminated hair, wool, hides, flesh, blood and excreta of infected animals and from manufactured products such as bone meal. Infection is introduced through scratches or abrasions of the skin, wounds, inhalation of spores, eating insufficiently cooked infected meat, or by biting flies. The primary concern for intentional infection by this organism is through inhalation after aerosol dissemination of spores. All human populations are susceptible. The spores are very stable and may remain viable for many years in soil and water. They resist sunlight for varying periods.

   b. **Brucellosis:** Brucellosis is one of the world's most important veterinary diseases, and is caused by infection with one of six species of Brucellae, a group of gram-negative cocco-baccillary facultative intracellular pathogens. In animals, brucellosis primarily involves the reproductive tract, causing septic abortion and orchitis, which, in turn, can result in sterility. Consequently, brucellosis is a disease of great potential economic impact in the animal husbandry industry. Four species (B. abortus, B. melitensis, B. suis, and, rarely, B. canis) are pathogenic in humans. Infections in abattoir and laboratory workers suggest that the Brucellae are highly infectious via the aerosol route. It is estimated that inhalation of only 10 to 100 bacteria is sufficient to cause disease in man.

   c. **Glanders and Melioidosis:** The causative agents of Glanders and Melioidosis are Burkholderia mallei and Burkholderia pseudomallei, respectively. Both are gram-negative bacilli with a "safety-pin" appearance on microscopic examination. Both pathogens affect domestic and wild animals, which, like humans, acquire the diseases from inhalation or contaminated injuries. B. mallei is primarily noted for producing disease in horses, mules, and donkeys. In the past man has seldom been infected, despite frequent and often close contact with infected animals. This may be the result of exposure to low concentrations of organisms from infected sites in ill animals and because strains virulent for equids are often less virulent for man. There are four basic forms of

disease in horses and man. The acute forms are more common in mules and donkeys, with death typically occurring 3 to 4 weeks after illness onset. The chronic form of the disease is more common in horses and causes generalized lymphadenopathy, multiple skin nodules that ulcerate and drain, and induration, enlargement, and nodularity of regional lymphatics on the extremities and in other areas. The lymphatic thickening and induration has been called farcy. Human cases have occurred primarily in veterinarians, horse and donkey caretakers, and abattoir workers. B. pseudomallei is widely distributed in many tropical and subtropical regions. The disease is endemic in Southeast Asia and northern Australia. In northeastern Thailand, B. pseudomallei, is one of the most common causative agents of community-acquired septicemia. Melioidosis presents in humans in several distinct forms, ranging from a subclinical illness to an overwhelming septicemia, with a 90% mortality rate and death within 24–48 hours after onset. Also, melioidosis can reactivate years after primary infection and result in chronic and life-threatening disease. These organisms spread to man by invading the nasal, oral, and conjunctival mucous membranes, by inhalation into the lungs, and by invading abraded or lacerated skin. Aerosols from cultures have been observed to be highly infectious to laboratory workers. Biosafety level 3 containment practices are required when working with these organisms in the laboratory. Since aerosol spread is efficient, and there is no available vaccine or reliable therapy, B. mallei and B. pseudomallei have both been viewed as potential BW agents.

d. **Plague:** Yersinia pestis is a rod-shaped, non-motile, non-sporulating, gram-negative bacterium of the family Enterobacteraceae. It causes plague, a zoonotic disease of rodents (e.g., rats, mice, ground squirrels). Fleas that live on the rodents can transmit the bacteria to humans, who then suffer from the bubonic form of plague. The bubonic form may progress to the septicemic and/or pneumonic forms. Pneumonic plague would be the predominant form after a purposeful aerosol dissemination. All human populations are susceptible. Recovery from the disease is followed by temporary immunity. The organism remains viable in water, moist soil, and grains for several weeks. At near freezing temperatures, it will remain alive from months to years but is killed by 15 minutes of exposure to 55°C. It also remains viable for some time in dry sputum, flea feces, and buried bodies but is killed within several hours of exposure to sunlight.

e. **Q-Fever:** The endemic form of Q fever is a zoonotic disease caused by the rickettsia, Coxiella burnetii. Its natural reservoirs are sheep, cattle, goats, dogs, cats and birds. The organism grows to especially high concentrations in placental tissues. The infected animals do not develop the disease, but do shed large numbers of the organisms in placental tissues and body fluids including milk, urine, and feces. Exposure to infected animals at parturition is an important risk factor for endemic disease. Humans acquire the disease by inhalation of aerosols

contaminated with the organisms. Farmers and abattoir workers are at greatest risk occupationally. A biological warfare attack with Q fever would cause a disease similar to that occurring naturally. Q fever is also a significant hazard in laboratory personnel who are working with the organism.

f. **Tularemia:** Francisella tularensis, the causative agent of tularemia, is a small, aerobic non-motile, gram-negative cocco-bacillus. Tularemia (also known as rabbit fever and deer fly fever) is a zoonotic disease that humans typically acquire after skin or mucous membrane contact with tissues or body fluids of infected animals, or from bites of infected ticks, deerflies, or mosquitoes. Less commonly, inhalation of contaminated dusts or ingestion of contaminated foods or water may produce clinical disease. Respiratory exposure by aerosol would typically cause typhoidal or pneumonic tularemia. F. tularensis can remain viable for weeks in water, soil, carcasses, hides, and for years in frozen rabbit meat. It is resistant for months to temperatures of freezing and below. It is easily killed by heat and disinfectants.

g. **Smallpox:** Smallpox is caused by the Orthopox virus, variola, which occurs in at least two strains, variola major and the milder disease, variola minor. Despite the global eradication of smallpox and continued availability of a vaccine, the potential weaponization of variola continues to pose a military threat. This threat can be attributed to the aerosol infectivity of the virus, the relative ease of large-scale production, and an increasingly Orthopoxvirus-naive populace. Although the fully developed cutaneous eruption of smallpox is unique, earlier stages of the rash could be mistaken for varicella. Secondary spread of infection constitutes a nosocomial hazard from the time of onset of a smallpox patient's exanthem until scabs have separated. Quarantine with respiratory isolation should be applied to secondary contacts for 17 days post-exposure. Vaccinia vaccination and vaccinia immune globulin each possess some efficacy in post-exposure prophylaxis.

h. **Venezuelan Equine Encephalitis:** The Venezuelan equine encephalitis (VEE) virus complex is a group of eight mosquito-borne alphaviruses that are endemic in northern South America and Trinidad and causes rare cases of human encephalitis in Central America, Mexico, and Florida. These viruses can cause severe diseases in humans and Equidae (horses, mules, burros, and donkeys). Natural infections are acquired by the bites of a wide variety of mosquitoes. Equidae serve as amplifying hosts and source of mosquito infection. Western and Eastern Equine Encephalitis viruses are similar to the VEE complex, are often difficult to distinguish clinically, and share similar aspects of transmission and epidemiology. The human infective dose for VEE is considered to be 10-100 organisms, which is one of the principal reasons that VEE is considered a militarily effective BW agent. Neither the population density of infected mosquitoes nor the aerosol concentration of virus particles has to be great to allow

significant transmission of VEE in a BW attack. There is no evidence of direct human-to-human or horse-to-human transmission. Natural aerosol transmission is not known to occur. VEE particles are not considered stable in the environment, and are thus not as persistent as the bacteria responsible for Q fever, tularemia or anthrax. Heat and standard disinfectants can easily kill the VEE virus complex.

i. **Viral Hemorrhagic Fevers (VHF):** The viral hemorrhagic fevers are a diverse group of illnesses caused by RNA viruses from four viral families. The Arenaviridae include the etiologic agents of Argentine, Bolivian, and Venezuelan hemorrhagic fevers, and Lassa fever. The Bunyaviridae include the members of the Hantavirus genus, the Congo-Crimean hemorrhagic fever virus from the Nairovirus genus, and the Rift Valley fever virus from the Phlebovirus genus; the Filoviridae include Ebola and Marburg viruses; and the Flaviviridae include dengue and yellow fever viruses. These viruses are spread in a variety of ways; some may be transmitted to humans through a respiratory portal of entry. Although evidence for weaponization does not exist for many of these viruses, they are included in this handbook because of their potential for aerosol dissemination or weaponization, or likelihood for confusion with similar agents that might be weaponized.

j. **Botulinum:** The botulinum toxins are a group of seven related neurotoxins produced by the spore-forming bacillus Clostridium botulinum and two other Clostridia species. These toxins, types A through G, are the most potent neurotoxins known; paradoxically, they have been used therapeutically to treat spastic conditions (strabismus, blepharospasm, torticollis, tetanus) and cosmetically to treat wrinkles. The spores are ubiquitous; they germinate into vegetative bacteria that produce toxins during anaerobic incubation. Industrial-scale fermentation can produce large quantities of toxin for use as a BW agent. There are three epidemiologic forms of naturally occurring botulism: food borne, infantile, and wound. Botulinum could be delivered by aerosol or used to contaminate food or water supplies. When inhaled, these toxins produce a clinical picture very similar to food borne intoxication, although the time to onset of paralytic symptoms after inhalation may actually be longer than for food borne cases, and may vary by type and dose of toxin. The clinical syndrome produced by these toxins is known as “botulism.”

k. **Ricin:** Ricin is a potent protein cytotoxin derived from the beans of the castor plant (Ricinus communis). Castor beans are ubiquitous worldwide, and the toxin is fairly easy to extract; Therefore, ricin is potentially widely available. When inhaled as a small particle aerosol, this toxin may produce pathologic changes within 8 hours and severe respiratory symptoms followed by acute hypoxic respiratory failure in 36–72 hours. When ingested, ricin causes severe gastrointestinal symptoms followed by vascular collapse and death. This toxin may also cause disseminated

intravascular coagulation, microcirculatory failure and multiple organ failure if given intravenously in laboratory animals.

l. **Staphylococcal Enterotoxin B:** Staphylococcus aureus produces a number of exotoxins, one of which is Staphylococcal enterotoxin B, or SEB. Such toxins are referred to as exotoxins since they are excreted from the organism, and because they normally exert their effects on the intestines they are called enterotoxins. SEB is one of the pyrogenic toxins that commonly causes food poisoning in humans after the toxin is produced in improperly handled foodstuffs and subsequently ingested. SEB has a very broad spectrum of biological activity. This toxin causes a markedly different clinical syndrome when inhaled than it characteristically produces when ingested. Significant morbidity is produced in individuals who are exposed to SEB by either portal of entry to the body.

m. **T-2 Mycotoxins:** The trichothecene (T-2) mycotoxins are a group of over 40 compounds produced by fungi of the genus Fusarium, a common grain mold. They are small molecular weight compounds, and are extremely stable in the environment. They are the only class of toxin that is dermally active, causing blisters within a relatively short time after exposure (minutes to hours). Dermal, ocular, respiratory, and gastrointestinal exposures would be expected after an attack with mycotoxins.

BWP-L LITERATURE

OUTCOME: The patient/family will receive literature about exposure to biological weapons.

STANDARDS:

1. Provide the patient/family with literature on biological weapons.
2. Discuss the content of the literature.

BWP-LA LIFESTYLE ADAPTATIONS

OUTCOME: The patient/family will strive to make lifestyle adaptations necessary to limit exposure, prevent complications and prevent the spread of exposure to biological weapons as appropriate.

STANDARDS:

1. Review lifestyle aspects/changes that the patient has control over diet, exercise, safety, injury prevention, avoidance of high-risk behaviors, and fully participating in a treatment plan.
2. Emphasize that an important component in the prevention or treatment of exposure to biological weapons is the patient's adaptation to a healthier, lower risk lifestyle.

3. Emphasize that an important component in the preventing the spread of exposure to biological weapons is the patient's adaptation to a healthier, lower risk lifestyle as appropriate.
4. Emphasize that if patient/family believe that there has been exposure with a biological weapon they should contact a healthcare professional for advice Usually the patient should remain where they are and fully participate with recommendations in order to limit the possibility of spreading the disease as appropriate.
5. Review the community resources available to assist the patient in making lifestyle changes. Refer as appropriate.

BWP-M MEDICATIONS

OUTCOME: The patient/family will understand the role of medications in the acute treatment of exposure, prophylaxis, and the prevention of disease resulting from exposure to biological weapons as appropriate.

STANDARDS:

1. Discuss the proper use, benefits, common side effects, and common interactions of prescribed medications. Review signs of possible toxicity and appropriate follow-up as indicated.
2. Review common side effects, signs of toxicity, and drug interactions of the medications.
3. Emphasize the importance of fully participating in the medication plan and explain how effective use of medications may reduce symptoms, complications, and prevent death.

BWP-P PREVENTION

OUTCOME: The patient/family will understand actions that may be taken to prevent exposure to and infection with biological warfare agents.

STANDARDS:

1. Instruct patient to avoid contact with people who are suspected of exposure to biological weapons.
2. Instruct patient on the importance of hand washing and maintaining appropriate hygiene.
3. Encourage patient to maintain natural resistance to infection through adequate nutrition, rest, and exercise.
4. Encourage patient to receive recommended medications and/or vaccinations for post-exposure prophylaxis and/or threat of biological agents as appropriate.

a. **Anthrax:** Oral antibiotics for known or imminent exposure. An FDA-licensed vaccine is available. Vaccine schedule is 0.5 ml SC at 0, 2, 4 weeks, then 6, 12, and 18 months (primary series), followed by annual boosters.

b. **Brucellosis:** There is no human vaccine available against brucellosis, although animal vaccines exist. Chemoprophylaxis is not recommended after possible exposure to endemic disease. Treatment should be considered for high-risk exposure to the veterinary vaccine, inadvertent laboratory exposure, or confirmed biological warfare exposure.

c. **Glanders and Melioidosis:** Currently, no pre-exposure or post-exposure prophylaxis is available.

d. **Plague:** For asymptomatic persons exposed to a plague aerosol or to a patient with suspected pneumonic plague, appropriate course of antibiotic therapy or the duration of risk of exposure plus one week. No vaccine is currently available for plague prophylaxis. The previously available licensed, killed vaccine was effective against bubonic plague, but not against aerosol exposure.

e. **Q-Fever:** Chemoprophylaxis begun too early during the incubation period may delay but not prevent the onset of symptoms. Therefore, appropriate antibiotic therapy should be started 8–12 days post exposure and continued for 5 days. Antibiotic therapy has been shown to prevent clinical disease. An inactivated whole cell IND vaccine is effective in eliciting protection against exposure, but severe local reactions to this vaccine may be seen in those who already possess immunity. Therefore, an intradermal skin test is recommended to detect pre-sensitized or immune individuals.

f. **Tularemia:** A live, attenuated vaccine is available as an investigational new drug. It is administered once by scarification. A two-week course of tetracycline is effective as prophylaxis when given after exposure.

g. **Smallpox:** Immediate vaccination or revaccination should be undertaken for all personnel exposed.

h. **Venezuelan Equine Encephalitis:** A live, attenuated vaccine is available as an investigational new drug. A second, formalin-inactivated, killed vaccine is available for boosting antibody titers in those initially receiving the first vaccine. No post-exposure immunoprophylaxis. In experimental animals, alpha-interferon and the interferon-inducer poly-ICLC have proven highly effective as post-exposure prophylaxis. There are no human clinical data.

i. **Viral Hemorrhagic Fevers:** The only licensed VHF vaccine is yellow fever vaccine. Prophylactic ribavirin may be effective for Lassa fever, Rift Valley fever, CCHF, and possibly HFRS (available only as IND under protocol).

j. **Botulinum Toxin:** Pentavalent toxoid vaccine (types A, B, C, D, and E) is available as an IND product for those at high risk of exposure.

k. **Ricin:** There is currently no vaccine or prophylactic antitoxin available for human use, although immunization appears promising in animal models. Use of the protective mask is currently the best protection against inhalation.

l. **Staphylococcal Enterotoxin B:** Use of protective mask. There is currently no human vaccine available to prevent SEB intoxication.

m. **T-2 Mycotoxins:** The only defense is to prevent exposure by wearing a protective mask and clothing (or topical skin protectant) during an attack. No specific immunotherapy or chemotherapy is available for use in the field.

BWP-SM STRESS MANAGEMENT

OUTCOME: The patient will understand the role of stress management in bioterrorism.

STANDARDS:

1. Explain realistic information regarding bioterrorism threats in order to decrease the sense of crisis or anxiety that could arise from the threat or potential threat of biological weapons.
2. Discuss that stress from a threatened act of bioterrorism may be as great and as real as stress from an actual act of bioterrorism.
3. Explain that effective stress management may help reduce the anxiety associated with potential bioterrorism threats.
4. Discuss various stress management strategies such as becoming aware of your own reactions to stress, recognizing and accepting your limits, talking with people you trust about your worries or problems, practicing spiritual and cultural activities, and forming as well as practicing a plan.
5. Provide referrals as appropriate.

BWP-TE TESTS

OUTCOME: The patient/family will understand the role of testing in appropriate management of exposure to biological weapons.

STANDARDS:

1. Discuss why a microbiology culture may or may not be required to confirm diagnosis of a biological weapon.
2. Explain what test(s) will be ordered. Provide information on the indication, benefits, and risks of the tests.
3. Explain how test results will be used to guide therapy.

BWP-TX TREATMENT

OUTCOME: The patient/family will understand the possible treatments available after exposure to a biological weapon.

STANDARDS:

1. Explain that the treatment plan will be made by patient and the healthcare team after reviewing available options
    a. **Anthrax:** Although effectiveness may be limited after symptoms are present, high dose antibiotic treatment should be undertaken. Supportive therapy may be necessary.
    b. **Brucellosis:** Antibiotic therapy in combination with other medications for six weeks is usually sufficient in most cases. More prolonged regimens may be required for patients with complications of meningoencephalitis, endocarditis, or osteomyelitis.
    c. **Glanders and Melioidosis:** Therapy will vary with the type and severity of the clinical presentation. Patients with localized disease, may be managed with oral antibiotics for a duration of 60–150 days. More severe illness may require parenteral therapy and more prolonged treatment.
    d. **Plague:** Early administration of antibiotics is critical, as pneumonic plague is invariably fatal if antibiotic therapy is delayed more than one day after the onset of symptoms.
    e. **Q-Fever:** Q fever is generally a self-limited illness even without treatment, but antibiotic therapy should be provided to prevent complications of the disease. Q fever endocarditis (rare) is much more difficult to treat.
    f. **Tularemia:** Administration of antibiotics with early treatment is very effective.
    g. **Smallpox:** At present there is no effective chemotherapy, and treatment of a clinical case remains supportive.
    h. **Venezuelan Equine Encephalitis:** Treatment is supportive only. Treat uncomplicated VEE infections with analgesics to relieve headache and myalgia. Patients who develop encephalitis may require anticonvulsants and intensive supportive care to maintain fluid and electrolyte balance, ensure adequate ventilation, and avoid complicating secondary bacterial infections.
    i. **Viral Hemorrhagic Fevers:** Intensive supportive care may be required. Antiviral therapy with ribavirin may be useful in several of these infections (available only as IND under protocol). Convalescent plasma may be effective in Argentine hemorrhagic fever (available only as IND under protocol).

j. **Botulinum Toxin:** Early administration of trivalent licensed antitoxin or heptavalent antitoxin (IND product) may prevent or decrease progression to respiratory failure and hasten recovery. Intubation and ventilatory assistance for respiratory failure. Tracheostomy may be required.

k. **Ricin:** Management is supportive and should include treatment for pulmonary edema. Gastric lavage and cathartics are indicated for ingestion, but charcoal is of little value for large molecules such as ricin.

l. **Staphylococcal Enterotoxin B:** Treatment is limited to supportive care. Artificial ventilation might be needed for very severe cases, and attention to fluid management is important.

m. **T-2 Mycotoxin:** There is no specific antidote. Treatment is supportive. Soap and water washing, even 4–6 hours after exposure can significantly reduce dermal toxicity; washing within 1 hour may prevent toxicity entirely. Superactivated charcoal should be given orally if the toxin is swallowed.